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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,321	03/05/2001	Muralidhara Padigaru	15966-703 (Cura-203)	2997

7590 03/22/2004

INTELLECTUAL PROPERTY
CuraGen Corporation
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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/800,321	PADIGARU ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,36,39 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,36,39 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05 January 2004 has been entered.

Claims 1, 36, 39, and 57 are pending and examined on merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

This Office action contains new grounds of rejection.

Claim Rejections - 35 USC § 101

Claims 1, 36, 39, and 57 remain rejected for reason of record under 35 U.S.C. 101 because the claimed invention is not supported by substantial asserted utility or a well established utility.

Claims 1, 36, and 39 are drawn to an isolated protein comprising SEQ ID NO:4 protein (claim 1), composition comprising said protein as the main ingredient (claim 36), and a kit comprising said composition. Claim 57 is drawn to an isolated polypeptide comprising fragment of SEQ ID NO:4 i.e. amino acid residues 39-313 of SEQ ID NO:4.

Applicant argues with the data presented in the Dr. Jeffers' declaration filed 05 January 2004. However, the declaration under 37 CFR 1.132 filed 05 January 2004 is

insufficient to overcome the rejection of claims 1, 36, 39, and 57 based upon lack of utility under 35 U.S.C. 101 and insufficiency of disclosure under 35 U.S.C. 112, first paragraph as set forth in the last Office action because: the facts presented in the declaration filed on 05 January 2004 are not germane to the rejection at issue.

The Office action mailed on 11/06/2002 stated that the specification does not show whether the claimed polypeptide is overexpressed or underexpressed in a specific, diseased tissue compared to the healthy tissue control. The Office action mailed on 7/3/2003 stated at page 3 that applicant is invited to present data the claimed protein overexpression is correlated with in vivo cancer or any other disease to obviate this rejection.

However, the data in Table 1 of the declaration is *in vitro* demonstration of the protein expression in certain cancer cell lines, namely T47D, MCF7, OVCAR-3. Dr. Jeffers' declaration at the Paragraph 6 of page 2 states that the Results in Table 1 shows that breast cancer cell lines T47D, MCF7, and ovarian carcinoma cell line OVCAR-3 were found to express polypeptide SEQ ID NO:4 as detected by anti-SEQ ID NO:4 polyclonal antibody. T47D, MCF7, or OVCAR-3 expresses a higher level of SEQ ID NO:4 protein as compared to the expression level of SEQ ID NO:4 protein of ACHN cell line (the last column in Table 1) which previously was shown not to express nucleic acid encoding SEQ ID NO:4. Applicant's argument, and Dr. Jeffers' declaration along with the data presented in Table 1 have been fully considered but found unpersuasive. The art recognizes that in vitro data do not correlate to in vivo data because the characteristics of cultured cell lines generally differ significantly from the characteristics

of in vivo primary cancers or metastatic cancers. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, page 4) teach that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary -type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not, yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Thus, based on the cell culture data presented in the declaration, it could

not be predicted that either SEQ ID NO:4 or its fragment could be overexpressed in vivo cancers.

Therefore, the disclosed utilities are not considered specific, credible, and substantial because they are just invitations for one skilled in the art to figure out how the protein functions or what the biological activities are for the claimed invention. It is noted that law requires that the disclosure of an application shall inform those skilled in the art how to use applicants' alleged discovery, not how to find out how to use it for themselves. The instant application has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a credible, specific and substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed protein. "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner v. Manson*, 148 USPQ at 696.

35 U.S.C. § 112, First Paragraph

Claims 1, 36, 39, 57 remain rejected for reason of record under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know ***how to use*** the claimed invention.

The Following Are New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claim 57 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim is interpreted as drawn to a genus of an isolated polypeptide comprising a fragment of SEQ ID NO:4 i.e. amino acid residues 39-313 of SEQ ID NO:4. The specification teaches only one species, SEQ ID NO:4. The specification does not teach any other species comprising amino acid residues 39-313 of SEQ ID NO:4. The specification does not teach what the function of the claimed genus must have. The claim encompasses other unpredictable species such as different allelic variant at the N-terminal end.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure, a fragment of a human protein. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, given that the specification has only described SEQ ID NO: 4. Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. This rejection would be obviated by reciting a function of the claimed genus must possess.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

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SUPERVISORY PATENT EXAMINER
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